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Decellularization as a method to generate a new generation of vascular grafts

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i Koferensrummet plan 5, Biotech Center, Arvid Wallgrens Backe 20, 413 46 Göteborg, den 9 Juni 2020, klockan 13:00.

av Robin Simsa

Fakultetsopponent
Dr. Nicolas L'Heureux
Université de Bordeaux, Frankrike

Avhandlingen baseras på följande delarbeten

I. Robin Simsa, Arvind Manikantan Padma, Philipp Heher, Mats Hellström, Andreas Teuschl, Lachmi Jenndahl, Niklas Bergh, Per Fogelstrand. Systematic in vitro comparison of decellularization protocols for blood vessels. PLoS One. 2018 Dec 17;13(12):e0209269. doi: 10.1371/journal.pone.0209269. PMID: 30557395; PMCID: PMC6296505.

II. Robin Simsa, Xavier Monforte Vila, Elias Salzer, Andreas Teuschl, Lachmi Jenndahl, Niklas Bergh, Per Fogelstrand. Effect of fluid dynamics on decellularization efficacy and mechanical properties of blood vessels. PLoS One. 2019;14(8):e0220743. Published 2019 Aug 5. doi:10.1371/journal.pone.0220743

III. Joakim Håkansson, Robin Simsa, Yalda Bogestål, Lachmi Jenndahl, Tobias Gustafsson-Hedberg, Raimund Strehl, Klas Österberg. Personalized tissue-engineered veins as vascular graft transplants: a proof of concept study in pig. Submitted to Journal (Manuscript)

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Decellularization as a method to generate a new generation of vascular grafts

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Abstract

Decellularization of blood vessels is a technique to remove cells from the extracellular matrix (ECM), which can be used as a vascular graft for peripheral or coronary blood vessel bypass surgery. This thesis focuses on the optimization of decellularization strategies for blood vessels such as porcine *vena cava*, to determine the optimal decellularization protocol (Paper I) and the ideal method of applying liquids during the decellularization process (Paper II). Our optimized strategy for blood vessel decellularization, which removes all cells from the ECM but leaves the mechanical properties and ultrastructure of the ECM intact, employs the detergents TritonX-100 and Tri-n-butyl phosphate in combination with the enzyme DNase, applied either by agitation or perfusion at low velocities. To test the utility of the decellularized vascular grafts, a preclinical animal study was performed by transplanting *vena cava* grafts in a pig animal model (Paper III). This study utilized decellularized blood vessels that were reconditioned with whole peripheral blood before transplantation. The results showed that blood vessels remained patent, resisted mechanical pressure and did not lead to a major immunogenic response. Taken together, this thesis describes a promising technique to generate novel vascular grafts based on decellularization on reconditioning of the ECM.

Keywords: Decellularized vascular graft, Tissue engineering, Reconditioning, Preclinical animal models, Reendothelialization

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